

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CA2004/002142

## 13. CLASSIFICATION OF SUBJECT MATTER

According to International Patent Classification (IPC) or to both national classification and IPC  
IPC: A61K38/18, A61K31/198, A61K31/04, A61P01/00

## 14. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC: A61K38/18, A61K31/198, A61K31/04, A61P01/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)

MEDLINE, CAPLUS, BIOSIS, DELPHION, CANADIAN PATENT DATABASE

Keywords: necrotizing enterocolitis, nitric oxide, arginine, glutamine, ornithine ketoglutarate, EGF, epidermal factor

## 15. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No(s).
Y	WO 01 30340 A1 (PROBIOTIX INC.) 03-05-2001 Abstract, page 9 lines 22-24, page 10 lines 20-24 Example 3, Figure 7 Claims 1, 5, 13	1-60
Y	DVORAK et al.: "Epidermal growth factor reduces the development of necrotizing enterocolitis in a neonatal rat model". Am. J. Physiol. Gastrointest. Liver Physiol., January 2002, vol. 282, no.1, pages G156-G164 Abstract, page G156 right column, last sentence to page G157 left column line 2; page G158, right column; Figure 4; Table 2	1-60

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

\* Special categories of cited documents :  
"A" document defining the general state of the art which is not considered to be of particular relevance  
"E" earlier application or patent but published on or after the international filing date  
"L" document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  
"O" document referring to an oral disclosure, use, exhibition or other means  
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone  
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art  
"&" document member of the same patent family

Date of the actual completion of the international search  
4 February 2005 ( 04-02-2005)

Date of mailing of the international search report  
22 March 2005 (22-03-2005)

Name and mailing address of the ISA/CA  
Canadian Intellectual Property Office  
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## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No(s).
Y	SULLIVAN et al.: "Epidermal growth factor in necrotising enteritis". Lancet, 6 July 1991, vol. 338, no. 8758, pages 53-54 whole document	1-60
Y	DILSIZ et al.: "Enteral glutamine supplementation and dexamethasone attenuate the local intestinal damage in rats with experimental necrotizing enterocolitis". Pediatr. Surg. Int., 11 October 2003, vol. 19, no. 8, pages 578-582 Abstract; Figure 1; Table 2	1-60
Y	DI LORENZO et al.: "Use of L-arginine in the treatment of experimental necrotizing enterocolitis". J. Pediatric Surg., February 1995, vol. 30, no. 2, pages 235-241 Abstract; page 236, left column, 1st and 2 <sup>nd</sup> full paragraphs; page 237, right column, 3 <sup>rd</sup> full paragraph; page 239, right column, 2 <sup>nd</sup> full paragraph Figure 2	1-60
Y	AMIN et al.: "Arginine supplementation prevents necrotizing enterocolitis in the premature infant". J. Pediatrics, April 2002, vol. 140, no. 4, pages 425-431 Abstract; page 427 last paragraph to page 428, left column line 5; Discussion, 1 <sup>st</sup> paragraph	1-60

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## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons :

7. ☒ Claim Nos. : 9, 23-31 and 41-60  
because they relate to subject matter not required to be searched by this Authority, namely :

Claims 23-31 and 41-46, directed to a method of treatment of the human/animal body, are not required to be searched by this Authority under Rule 39.1 (iv) PCT. With respect to claims 9 and 47-60, these claims are written in a "composition for treating a medical condition" format. No unified criteria exists in the PCT for claims in such format. The Canadian Intellectual Patent Office, for example, allows claims written in such a format, however, not all designated states do. Thus, claims 9 and 47-60 are also considered to be directed to a method of treatment of the human/animal body, are not required to be searched by this Authority under Rule 39.1 (iv) PCT.

Regardless, a search has been carried out and based on the alleged effects of the products defined in claims 9, 23-31 and 41-60.

8. ☒ Claim Nos. : 1-60  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically :

The term "bioequivalent" in claims 1, 10, 17, 23-24, 27, 32, 42, 45, 47, 50, 56 and 59 and the expression "capable of increasing the in vivo generation of NO" in claims 41, 44, 55 and 58 do not comply with Article 6 PCT because they may relate to an extremely large number of possible products due to the fact that they define the products by function or desired result. Consequently, the search has been carried out for the parts of the application which appear to be clear in this regard, namely the L-arginine, L-citrulline, ornithine alpha-ketoglutarate or glutamine (see page 6 lines 32-35).

Claims 1-8, 10-22, 32 and 34-40 do not comply with Article 5 PCT and Article 6 PCT because the products defined in these claims are not restricted to a particular use or method. The application provides support within the meaning of Article 6 PCT and description within the meaning of Article 5 PCT for the use of the claimed products for a specific medical application, namely necrotizing enterocolitis and therefore the search has been carried out for the claimed products as they relate to said specific medical application.

9. ☐ Claims Nos. :  
because they are dependant claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows :

- ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
10. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
11. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos. :
12. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos. :

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

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Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
WO0130340 A1	03-05-2001	AU1130300 A CA2388724 A1 EP1244439 A1 JP2003521481T T US5981590 A	08-05-2001 03-05-2001 02-10-2002 15-07-2003 09-11-1999